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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/627,206	07/27/2000	Jane A. Gross	98-75C2	1238

7590 03/03/2004

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EXAMINER

ZEMAN, ROBERT A

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 03/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/627,206

Applicant(s)

GROSS, JANE A.

Examiner

Robert A. Zeman

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 31 October 2003. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☒ Applicant's reply has overcome the following rejection(s): see attached.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____

Claim(s) objected to: _____

Claim(s) rejected: 89 and 102-111.

Claim(s) withdrawn from consideration: _____

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
10. ☐ Other: _____

ADVISORY ACTION

Terminal Disclaimer

The terminal disclaimer filed on 10-31-2003 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted in Application 09/569,245 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections Withdrawn

The provisional rejection of claims 89 and 102-111 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 64-96 of copending Application No. 09/569,245 is withdrawn in light of the Terminal Disclaimer filed on 10-31-2003.

The rejection of claims 105-106 under 35 U.S.C. 112, second paragraph as being rendered vague and indefinite by the use of the phrase "the composition comprises multimeric proteins comprising one or more fusion proteins" is withdrawn in light of the amendment thereto.

The rejection of claims 110-111 under 35 U.S.C. 112, second paragraph as being rendered vague and indefinite by the use of the phrase "the composition comprises dimeric proteins comprising one or more fusion proteins" is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The instant claims are drawn to methods of inhibiting B cell proliferation by the administration of a soluble form the ztnf4 receptor (TACI). Said soluble form of the ztnf4 receptor can comprise the extracellular domain of the TACI protein and may be optionally fused to the heavy chain constant region of human immunoglobulins.

The rejection of claims 89, 102 and 107 under 35 U.S.C. 102(a) as being anticipated by Bram et al. (WO 98/39361 – IDS-5) is maintained for reasons of record.

The rejection of claims 89, 102 and 107 under 35 U.S.C. 102(e) as being anticipated by Bram et al. (U.S. Patent 5,969,102 – IDS-5) is maintained for reasons of record.

Applicant argues:

1. The instant invention requires binding to the ligand ztnf4.
2. Bram et al. do not disclose the identity of the endogenous ligand of the TACI protein.

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3. The instant claims are drawn to a method of use not a composition.
4. Disclosure of a receptor does not inherently disclose the identity of its ligand or that ligand's activity.
5. It would have required undue experimentation to determine that B cell proliferation caused by ztnf4 is inhibited through the administration of the recited TACI fusion proteins.

Applicant's arguments have been fully considered and deemed non-persuasive.

As outlined previously, s Since compositions (i.e. ztnf4 receptor protein) disclosed by Bram et al. are identical to those of the instant invention, said compositions would possess all of the same properties as those of the instant invention (including the ability to bind ztnf4) and hence are deemed to be functional equivalents. Hence, Bram et al. anticipates all the limitations of the rejected claims. Moreover, previously, **Bram et al. disclose the use of genetically engineered constructs to regulate B-cell activity through its interaction with cellular receptor ligands (i.e. ztnf4).** Said constructs can consist of the extracellular domain of the TACI receptor fused to the Fc domain of an immunoglobulin (see page 24, lines 24-26). Bram et al. further disclose that said extracellular domain has an amino acid sequence corresponding to about residue 1 to about residue 166 of the consensus sequence of TACI and that the ligand binding region is a sub-fragment of the extracellular domain (see page 18, lines 27-30).

With regard to points 2-5, Applicant is reminded that under the principles of inherency, if a prior art device, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art device. When the prior art device is the same as a device described in the specification for carrying out

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the claimed method, it can be assumed the device will inherently perform the claimed process. *In re King*, 801 F.2d 1324, 231 USPQ 136 (Fed. Cir. 1986). Additionally Applicant is reminded “the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best* 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The instant claims are drawn to methods of inhibiting B cell proliferation by the administration of a soluble form the ztnf4 receptor (TACI). Said soluble form of the ztnf4 receptor can comprise the extracellular domain of the TACI protein that is optionally fused to the

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heavy chain constant region of human immunoglobulins. Additionally, said soluble form of the ztnf4 may comprise a dimer or other multimer of said fusion protein

The rejection of claims 89 and 102-111 under 35 U.S.C. 103(a) as being unpatentable over Bram et al. (WO 98/39361 – IDS-5), as cited above, in view of Presta et al. (U.S. Patent 5,739,277) is maintained for reasons of record.

Applicant argues:

1. The instant invention requires binding to the ligand ztnf4.
2. Bram et al. do not disclose the identity of the endogenous ligand of the TACI protein.
3. The disclosure by Presta et al. is insufficient to overcome the aforementioned deficiency.
4. The instant claims are drawn to a method of use not a composition.
5. Disclosure of a receptor does not inherently disclose the identity of its ligand or that ligand's activity.
6. It would have required undue experimentation to determine that B cell proliferation caused by ztnf4 is inhibited through the administration of the recited TACI fusion proteins.

Applicant's arguments have been fully considered and deemed non-persuasive.

As outlined previously, since compositions (i.e. ztnf4 receptor protein) disclosed by Bram et al. are identical to those of the instant invention, said compositions would possess all of the same properties as those of the instant invention (including the ability to bind ztnf4) and hence are deemed to be functional equivalents. Moreover, **Bram et al. disclose the use of genetically engineered constructs to regulate B-cell activity through its interaction with cellular**

receptor ligands (i.e. ztnf4). Said constructs can consist of the extracellular domain of the TACI receptor fused to the Fc domain of an immunoglobulin (see page 24, lines 24-26). Bram et al. further disclose that said extracellular domain has an amino acid sequence corresponding to about residue 1 to about residue 166 of the consensus sequence of TACI and that the ligand binding region is a sub-fragment of the extracellular domain (see page 18, lines 27-30). Bram et al. differs from the instant invention (claims 103-104 and 108-109) in that they do not disclose the specific use of human IgG1 heavy chains in fusion proteins. Presta et al. disclose methods of making fusion proteins comprising the Fc portion of a human immunoglobulin (including IgG1) and the advantages of making such proteins. Consequently, it would have been obvious to one of ordinary skill in the art to utilize the Fc portion of a human IgG1 molecule of Presta et al. in the fusion protein disclosed by Bram et al. in order to take care of the increased circulatory half life of said fusion proteins as disclosed by Presta et al. (see abstract). One would have had a high expectation of success since Presta et al. disclose that the Fc portions of the various immunoglobulins can be used interchangeably (see column 7, lines 3-45). Additionally, it would have been obvious to one of ordinary skill in the art to use said fusion protein in multimer form to increase the number of binding sites on the soluble form of the receptor.

With regard to points 2-6, With regard to Applicant's assertion that an obviousness rejection has to rely on what is taught by the art, not what is inherent in the art: Applicant is reminded that the express, implicit, and inherent disclosures of a prior art reference may be relied upon in the rejection of claims under 35 U.S.C. 102 or 103. "The inherent teaching of a prior art reference, a question of fact, arises both in the context of anticipation and obviousness." *In re Napier*, 55 F.3d 610, 613, 34 USPQ2d 1782, 1784 (Fed. Cir.1995) (affirmed a 35 U.S.C. 103

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rejection based in part on inherent disclosure in one of the references). See also *In re Grasselli*, 713 F.2d 731, 739, 218 USPQ 769, 775 (Fed. Cir. 1983). Under the principles of inherency, if a prior art device, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art device. When the prior art device is the same as a device described in the specification for carrying out the claimed method, it can be assumed the device will inherently perform the claimed process. *In re King*, 801 F.2d 1324, 231 USPQ 136 (Fed. Cir. 1986). Additionally Applicant is reminded "the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best* 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866.

The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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